Proptosis in Acute Myeloid Leukemia: An Under Recognized Presentation of Hematological Malignancy

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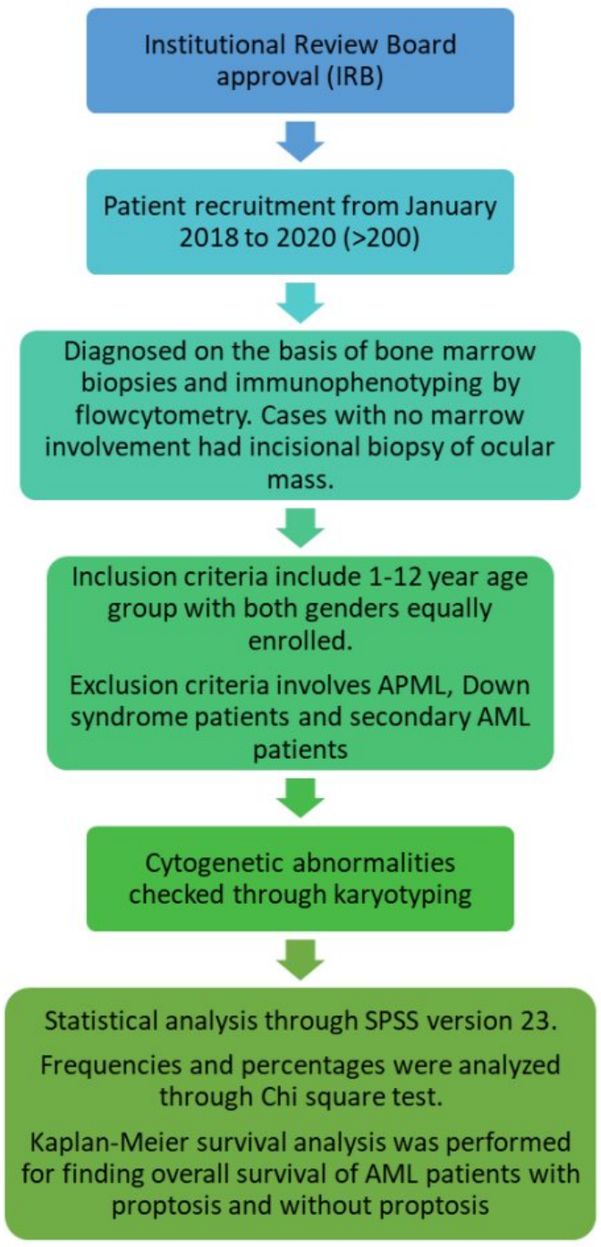
Introduction

Leukemia is the most common hematological malignancy in children [1]. Among all pediatric leukemia patients, 18% present with acute myeloid leukemia (AML) [2]. acute myeloid leukemia (AML). Fifty percent of all the pediatrics leukemia deaths have been attributed to AML with the survival rate of 64% in developed countries like United States [3]. Patients diagnosed with AML are extremely unfortunate as it not only exhausts the patient and their families physically and mentally but also have high financial implications. In the past AML was a difficult affliction to treat, but the treatment outcomes of pediatric AML have improved with advances in chemotherapy, hematopoietic stem cell transplantation and supportive care [4]. AML usually presents with systemic manifestations like blood dyscrasias and fever, but it can rarely present with extrame-dullary granulocytic sarcoma also known as myeloid sarcoma (MS) [5]. One of the most common sites of MS is the orbit which is also known as orbital granulocytic sarcoma (OGS) and can presents clinically as unilateral or bilateral proptosis [6]. This study was conducted to find out the frequency and associations of proptosis with demographic, clinical and hematological characteristics in children with AML.

Methodology



Results

TABLE I: Demographic and clinicopathological data of patients with orbital granulocytic sarcoma.

Variable		With Proptosis Frequency (%)	Without Proptosis Frequency (%)	Total Frequency (%)	P Value
Age distribution	< 5 years	13 (38.20)	82 (41.8)	95 (41.3)	0.406
	5-9 years	11 (32.4)	76 (38.8)	87 (37.8)	
	> 9 years	10 (29.4)	38 (19.4)	28 (20.9)	
Gender distribution	Males	23 (67.60)	123 (62.8)	146 (63.5)	0.584
	Females	11 (32.40)	73 (37.2)	84 (36.5)	
WBC count (cells/mm3)	<50,000	26 (76.5)	124 (63.3)	150 (65.2)	0.136
	³50,000	8 (23.5)	72 (36.7)	80 (34.8)	
Types of AML (FAB classification)	AML M2	26 (76.5)	76 (38.8)	102 (44.3)	0.001*
	others	8 (23.5)	122 (62.24)	128 (55.6)	
Total		34 (100)	196 (100)	230 (100)	

TABLE II: Systemic manifestation in patients with and without proptosis (n=217).

Systematic Manifestation		Proptosis Yes (%)	Proptosis No (%)	Proptosis Total (%)	P-Value
Fever	Yes	20 (58.8)	153 (83.6)	173 (79.7)	0.001*
	No	12 (41.2)	30 (16.4)	44 (20.3)	
Pallor	Yes	23 (67.6)	164 (89.6)	187 (86.2)	0.001*
	No	11 (32.4)	19 (10.4)	30 (13.8)	
Bruising	Yes	7 (20.6)	84(45.6)	91 (41.7)	0.007*
	No	27 (79.4)	99 (54.4)	126 (58.3)	
Bleeding	Yes	3 (8.8)	40 (21)	43 (19.1)	0.095
	No	31 (91.2)	143 (79)	174 (80.9)	
Lymphadenopathy	Yes	6 (17.6)	46 (24.7)	52 (23.6)	0.372
	No	28 (82.4)	137 (75.3)	165 (76.4)	
Bone Pains	Yes	5 (14.7)	29 (15.4)	34 (15.3)	0.92
	No	29 (85.3)	154 (84.6)	183 (84.7)	
Total		34 (100)	183 (100)	217 (100)	

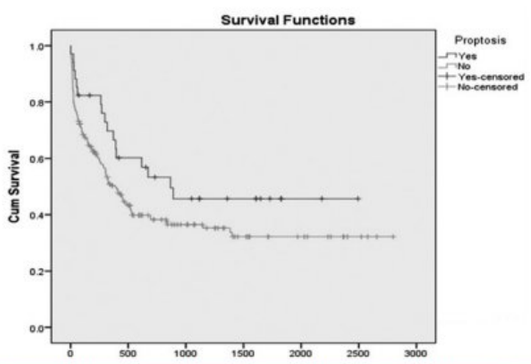


Figure 1: Kaplan Meier analysis curve

Discussion

In this study it was found that proptosis has a significant association with AML as 14.78% of our patients were found to have it. Proptosis presented not only with systemic features but also as an isolated phenomenon and can precede the onset of systemic AML. Presence of OGS with AML was found to be a **better prognostic** sign as median duration of survival in patients with OGS was found to be 867 days as compared to the 353 days in patients without OGS.

GS is a known association of AML reported in 2.5-9.1% of patients in literature.[9] These are tumors of immature hematopoietic precursor cells of granulocytic series which are localized in extra medullary tissues. Histological identification and diagnosis of these tumors in children is difficult and can easily be misinterpreted as malignant lymphomas or other common poorly differentiated pediatrics tumors like neuroblastoma and rhabdomyosarcoma especially when they precede the development of systemic leukemia.[10]

Proptosis is a frequent finding in children with AML. AML-M2 is associated with proptosis in children with AML.

Proptosis is an important sign of AML. Even in absence of systemic features patient should be promptly investigated for AML as proptosis can present as an isolated finding. This would require tissue biopsy and immunohistochemistry to prove or rule out AML.

Median age of presentation with GS in our study is 7 years compared to 11.6 months in patients as compared to other literature where age of presentation in pediatric population is between 6-8.8 years.

In our study male predominance was observed versus other studies that have reported female prelicdiction.

Cytogenetic abnormalities in our study associated with AML M2 (most common subtype) WAS t(8,21) responsible for AML ETO fusion, a finding found consistent during other literature review as well.t(8,21) is considered to be a good prognostic sign in some studies .

Overall survival of AML in our study was 50% which was lower than COG report where OS was 92%.Median duration of survival in our study in patients with OGS was 28.5 months compared to 11.6 months in patients of AML without OGS ,showing better survival associated with OGS whereas other studies show GS as a less favorable prognostic sign in AML associated with poor disease outcome, low remission rate overall survival and increased chance of relapse.it is recommended that proptosis is an important sign of AML, even with no systemic features patient should be promptly investigated to rule out AML.

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